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Title: JP7053391A2: COMPOSITION FOR TREATING IRON-DEFICIENC

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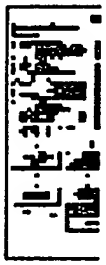

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Priority Number: Aug. 10, 1993 JP1993000218119

Abstract:

PURPOSE: To provide a composition for treating iron-deficiency anemia containing a fermented milk and an iron salt as the active ingredients, little in side effects, and useful for the therapy of iron-deficiency anemia.

CONSTITUTION: The composition for therapy of iron-deficiency anemia contains a fermented milk and a ferrous ion in an amount of 1-150mg per 100g or the fat-free milk solid content, the fermented milk being produced by inoculating a lactic acid bacterium belonging to the genus Lactobacillus acidophilus on a milk and subsequently fermenting the milk. The composition can be provided in the form of a food such as yogurt or in the form of tablets, capsules, powder, etc.

Family:

PDF	Patent	Pub. Date	Filed	Title
	JP7053391B4	June 7, 1995	Dec. 14, 1989	
	JP7053391A2	Feb. 28, 1995	Aug. 10, 1993	COMPOSITION FOR TREATING DEFICIENCY ANEMIA
	JP3184817A2	Aug. 12, 1991	Dec. 14, 1989	MULTI-LAYER TUBE JOINT

3 family members shown above

Other Abstract Info: DERABS C95-128252 DERC95-128252

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Accession Number

1995-128252 [17] WPINDEX

Title

Compsn. for therapy of ion-deficiency anaemia - comprising iron salt and milk prod. obtained with Lactobacillus acidophilus.

Patent Assignee

(SNOW) SNOW BRAND MILK PROD CO LTD

Patent Information

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Priority Application Information

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International Patent Classificatio

MAIN: A61K035-74

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Abstract

JP 07053391 A UPAB: 19950508

The compsn. for therapy of iron-deficiency anaemia comprises active constituents of milk fermented with the lactic-acid bacteria Lactobacillus acidophilus, and iron salt.

ADVANTAGE - Compsn. improves the efficiency of iron absorption. Unwanted effects and iron can be reduced. Minerals other than vitamins and iron can be also provided.

The fermented milk is prepd. by seeding Lactobacillus acidophilus in milk contg. 5-15 wt.% of non-fat milk solids and fermenting to lactic acidity of 0.1-2.0 wt.%.

EXAMPLE - 0.3 wt.% of yeast extract was added to skim milk contg. 11 wt.% of non-fat milk solids. The skim milk soln. was homogenized, then sterilized. Approx. 3 wt.% of Lactobacillus acidophilus SBT 2062 starter was added to the sterilized milk. The milk was fermented at 37 deg.C for 18 hrs. Lactic acidity of the fermented milk (yoghurt) was approx. 1.5%. 100 g of the yogurt was mixed with 5 g of ferrous citrate to prepare the iron-enriched yogurt.

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(54) [Name of the Invention] COMPOUND FOR THE TREATMENT OF IRON-DEFICIENCY ANEMIA

(57) [Summary of the Invention]

[Purpose] To provide a compound which is effective for the treatment of iron-deficiency anemia with few side-effects. Fermented milk and iron salts are its active ingredients.

[Construction] The compound for the treatment of iron-deficiency anemia contains fermented milk and ferrous ions in the proportion of 1 mg to 150 mg per 100 g of non-fat milk solids, the fermented milk being produced by introducing the lactic acid bacterium Lactobacillus acidophilus into the milk and subsequently fermenting that milk. The compound can be provided as a food product such as yoghurt, or as a food supplement in the form of tablets, capsules, or powder.

[Claims]

[Claim 1] The compound for the treatment of iron-deficiency anemia contains fermented milk and iron salts as its active ingredients, with the fermented milk being produced with the lactic acid bacterium Lactobacillus acidophilus.

[Claim 2] The fermented milk in the compound for the treatment of iron-deficiency anemia referred to in Claim 1 was produced by introducing the Lactobacillus acidophilus bacterium into milk with a non-fat milk solid content of between 5% and 15% by weight, and subsequently fermenting that milk, making the acidity level of lactic acid 0.1% to 2.0% by weight.

[Detailed Description of the Invention]

[0001]

[Industrially Applicable Field] This invention is a compound which is effective in the treatment of iron-deficiency anemia in human beings and in animals. Specifically, it is a compound for the treatment of iron-deficiency anemia containing fermented milk and iron salts as its active ingredients. The fermented milk is produced using the lactic acid bacterium Lactobacillus acidophilus.

[0002]

[Conventional Technology] Nowadays food supplies in Japan are abundant, and the average intake of most nutritional substances is above the National Recommended Intake. However, the average iron intake has for many years remained around the Recommended Intake level, with little change. Indeed, it is estimated that the average iron intake of almost half of the Japanese people is below the Recommended Intake level. These people need to take steps to increase their iron intake.

[0003] Chronic iron deficiency leads to iron-deficiency anemia, passing through a stage of latent sideropenia in which the symptoms of anemia do not appear. It is recognized that many adult women suffer from iron-deficiency anemia, with about a half of all adult women suffering from either iron-deficiency anemia or sideropenia.

[0004] The first choice remedy is to eat meat and fish which contain highly absorbent heme iron in order to reduce the symptoms of iron-deficiency anemia. However, the majority of patients suffering

from iron-deficiency anemia typically follow vegetarian-style diets, and this makes it difficult to increase their intake of foods containing iron without drastically changing their eating habits. There is one vegetable, though, which does contain a significant amount of iron, and that is spinach which is an excellent source of the mineral. Unfortunately, for the most part the iron in spinach is inorganic iron, the rate of absorption of which is below that of heme iron. It is in any case difficult to get anemic patients who already eat vegetarian meals to eat yet more vegetables like spinach.

[0005] Ordinarily, patients diagnosed with iron-deficiency anemia are recommended to take iron through means of tablets drug, or as iron-enriched foods. Regular, orally administered clinical treatments such as these, however, have produced side-effects such as anorexia, vomiting, abdominal pain, constipation and diarrhea. Constituents such as vitamin C are often administered concurrently in order to promote iron absorption. There are two kinds of iron: ferrous iron, which is easily absorbed and used; and ferric iron which is difficult to absorb and use, and which is found in inorganic iron. In regular iron drug the use of ferric iron decreases because the ferrous ions are partially changed to ferric irons by gastric acid, although vitamin C can be used to prevent this. However, the vitamin C must be administered in high doses because it is resolved easily by the gastric acid. When iron drugs and vitamin C are taken orally, the side-effects of the iron drugs; such as vomiting and epigastralgia increase.

[0006] In trials, milk casein and hydrolysate, an amino acid in pig liver, have been added to promote iron absorption. Casein phosphopeptide which is a hydrolysis product of casein, and Lactoferrin or Transferrin, which are iron binding proteins were administered. The association between casein and iron is registered in the official report ... 2-83400; iron drugs which contain Lactoferrin are registerdd in the official report ... 4-141067; and iron drugs which contain fungus bodies such as yeast are registered in the official report ... 3-291231.

[0007] The use of fermented milk products, such as yoghurt produced using lactic acid bacteria is known to have various physiological effects. Such products might therefore be expected to also have an effect on the treatment of iron-deficiency anemia. However, according to G. Schaafsma et.al, fermented milk produced with the lactic acid bacteria Lactobacillus bulgarics and Streptococcus thermopuilus prevents iron absorption and is thus not effective against iron-deficiency anemia.(G. Schaafsma et al., Neth. Milk Dairy J. and Vol. 42,135-146,1988).

[0008]

[Problem to be solved by this invention] Fermented milk products, such as yoghurt, which contain many proteins and which regulate the functions of the intestines are excellent nutritional supplementary foods. However, as noted in the above, it is not recommended that fermented milk is given to patients with iron-deficiency anemia because it is not effective and may have a negative effect on the patients. In the process of researching the physiological effects of fermented milk, the inventors found that fermented milk produced with the lactic acid bacterium Lactobacillus acidophilus

has the effect of promoting iron absorption, thus contradicting earlier findings. This is a new finding which is not yet fully understood, but the inventors did confirm that it depended on an action which was completely distinct from the effect produced by casein. Therefore, the purpose of this invention is to use fermented milk produced with the lactic acid bacterium Lactobacillus acidophilus, in order to improve the usability of iron, and to provide a compound for the treatment of iron-deficiency anemia without the side-effects associated with iron.

[0009]

[Solution of problem] This invention is a compound for the treatment of iron-deficiency anemia, containing fermented milk and iron salts as its active ingredients, the fermented milk being produced with the lactic acid bacterium Lactobacillus acidophilus. Though either an inorganic iron salt or an organic iron salt can be used, in terms of usability, a ferrous salt is desirable. Fermented milk can be used provided it is prepared using the lactic acid bacterium Lactobacillus acidophilus as a base, in the recognized method. It is preferable that the non-fat milk solid content is between 5% and 15% by weight, and that the level of acidity of the lactic acid bacteria is between 0.1% and 2.0% by weight. Dried powder made from milk thus fermented, such as freeze-dried powder or spray-dried powder can be used. The Lactobacillus acidophilus can be separated out from commercially available fermented milk, the bacterial strain subdivided from ATCC or IFO, or alternatively commercially available bases can be used.

[0010] The compound which constitutes this invention can be provided either in the form of a fermented milk product, such as regular yoghurt, or in the form of tablets or powder made from the dried powder of the fermented milk. Ferrous hydroxide, ferrous sulfate, ferrous orotate, threonine iron, soluble iron pyrophosphate, and ferrous sodium citrate can be used as the iron salt. Any iron salt other than those mentioned above can also be used for this product provided it is an iron salt used in the treatment of iron-deficiency anemia.

[0011] The compound which constitutes this invention can be boosted by the addition of vitamins and other inorganic constituents if necessary.

[0012] This invention usually contains between 1mg and 150 mg (10 mg to 100 mg being the preferred range) of iron content for every 100 g solid content of fermented milk produced with the lactic acid bacterium Lactobacillus acidophilus as a base. When the compound constituting this invention is used for the treatment of iron-deficiency anemia, the preferred dose is between 10 mg and 100 mg of iron, 1 to 3 times per day. The compound constituting this invention can be administered with a meal or between meals, though the preferred time is just after a meal. The dose can be adjusted in accordance with the patient's condition.

[0013] The compound constituting this invention could be provided in the form of a liquid food such as yoghurt or a drink, or as a powdered food product, but the possible adverse effect on the flavor by the iron salt must be taken into consideration. Consequently, as noted in the above, the compound

which constitutes this invention is best provided in the form of powder, tablets or capsules made from powdered fermented milk. For a binding agent, tragacanth gum, gum arabic, corn starch or gelatin, which are used for tablets and capsules would be suitable; for diluting agents, such as microcrystalline cellulose or magnesium stearate, and for swelling agents, such as corn starch or arginic acid would be suitable. Shellac and sugar can be used as the tablet coating.

[0014] It is acknowledged that the compound constituting this invention relieves the symptoms of iron-deficiency anemia, and improves the hemoglobin level of the blood remarkably. In particular, the symptoms of anemia were relieved significantly when the compound which constitutes this invention was compared with skimmed milk which main source of protein is casein, which also purports to have the effect of relieving the symptoms of anemia. This was confirmed using the following method. Rats with iron-deficiency anemia were prepared by feeding three-week old female Wistar rats for 13 days with the iron-deficient feed listed in Table 1. As a result, the average hemoglobin level of their blood dropped to 7.8 mg/dl. The hemoglobin level of normal rats is between 15 and 16 mg/dl.

[0015] These rats were then fed for seven days with the iron-mixed feed listed in Table 1. Ferrous sulfate salt was used as the source of iron.

[0016]

[Table 1]

Composition of Experiment Feed

Ingredient	Iron-deficient Feed	Iron-mixed Feed
Casein	20.0 (% by weight)	20.0 (% by weight)
DL-Methionine	0.3	0.3
Corn Oil	5.0	5.0
Saline Mixture 1	3.5	0
Saline Mixture 2	0	3.5
Vitamin Mixture	1.0	1.0
Choline Chloride	0.2	0.2
Cellulose	5.0	5.0
Corn Starch	65.0	65.0
Iron Content	4 ppm	22 ppm

[0017] The composition of saline mixture 1, saline mixture 2 and vitamin mixture listed in Table 1 are detailed in Table 2 and Table 3 below, and are in accordance with compound AIN76 based on the standards of the American Institute of Nutrition (J.Nutr., Vol.107,1340-1348 and 1977).

[0018]

[Table 2]

Composition of Saline Mixtures

Ingredient	Saline Mixture 1	Saline Mixture 2
	(% by weight)	(% by weight)
$CaHPO_4$	50	50
NaCl	7.4	7.4
$K_3C_6H_5O_7.H_2O$	22	22
K_2SO_4	5.2	5.2
MgO	2.4	2.4
$MnCO_3$	0.35	0.35
$FeSO_4$, $7H_2O$	0	0.29
$ZnCO_3$	0.16	0.16
$CuCO_3$, $Cu(OH)_2$, H_2O	0.03	0.03
Na_2SeO_3, 5H2O	0.001	0.001
KIO_2	0.001	0.001
$CrK(SO_4)_2$, $12H_2O$	0.055	0.055

The total is adjusted to 100% with cane sugar.

[0019]

[Table 3]

Composition of Vitamin Mixture

Ingredient	Content (per 100 g)
Vitamin A Acetate	40000 IU
Vitamin D_3	10000 IU
Vitamin E Acetate	500 mg
Vitamin K_3	0.5 mg
Vitamin B_1 Hydrochloride	60 mg
Vitamin B_3	60 mg
Vitamin B_6 Hydrochloride	70 mg
Vitamin B_{12}	0.1 mg

D-Biotin	2 mg
Pteroylglutamic Acid	20 mg
Calcium Pantothenate	160 mg
Nicotine Acid	300 mg

The total is adjusted to 100g with cane sugar.

[0020] The rats fed with the iron-mixed feed were divided into two groups (each group consisting of six rats). 2 ml of fermented milk prepared by the method shown in Detail 1 (below) was administered orally two times a day (total 4 ml) to the rats in the experiment group. Skimmed milk without the Lactobacillus acidophilus (also in Detail 1) was administered orally to the rats in the control group.

[0021] On the seventh day of the experiment period, blood was taken from their caudal veins and the hemoglobin level of that blood was measured in the usual way. The increase in hemoglobin levels after seven days were calculated for each rat by subtracting the hemoglobin level of the rats when suffering from iron-deficiency anemia at the start of the experiment period from their hemoglobin level on the seventh day of the experiment period. The increases in hemoglobin in blood are listed in Table 4.

[0022]

[Table 4]

Increases in hemoglobin levels

(Mean Value ± Standard Deviation)

	Increases in hemoglobin levels (mg/dl/7 days)
Experiment Group	4.6 ± 0.8
Control Group	4. 0± 0.6

[0023] A paired T-test on the increases in hemoglobin levels in the blood of the rats in the experiment group and the control group shows a significant difference between the two groups at a 95% level of significance. In other words, the group that was administered the fermented milk shows a significant relief in the symptoms of anemia in comparison with the group that was administered the skimmed milk. Table 5 shows the results of paired T-tests on the differences in body-weight gains of the experiment group and control group, and shows a significant difference between the two groups at a 95 % level of significance. However, paired T-tests on the food intake of the two groups shows no significant difference at the 95 % level of significance. It shows that there was no side-effect such as

the suppression of body-weight gain due to the intake of iron tablets in the experiment group. Accordingly, the body-weight gain of the control group was significantly lower than that of the experiment group.

[0024]

[Table 5]

Body-weight gain and food intake (Mean value ± Standard deviation)

	Sample Group	Control Group
Body-weight Gain (g/7 days)	32±4	26±6
Intake (g/7 days)	105±6	102±11

[0025] The technical details of the compound are given in the four Details below:

[Detail 1] UHT sterilization was carried out after adding 0.3% by weight of yeast extract to dried skimmed milk solution with a non-fat milk solid content of 11% by weight, and then homogenizing this solution. The fermented milk was prepared by adding 3% by weight of Lactobacillus acidophilus SBT2062 (Ministry of International Trade and Industry, Agency of Industrial Science Technology, National Institute of BioScience and Human-Technology, Submitted Number: ..... 10730 .) as a base, prepared in the usual way, to milk which had been pasteurized for 18 hours at 37ºC. The acidity level of the lactic acid contained in this fermented milk was about 1.5 %. The following compound was made from this yoghurt.

[0026]

[Detail 2] The iron-fortified yoghurt was prepared by adding 5 g of ferrous citrate to every 100 g of yoghurt prepared as in Detail 1.

[0027]

[Detail 3] The yoghurt prepared in Detail 1 was processed into a dried powder by freeze-drying. A 1000 tablets were prepared by evenly mixing 15 g of ferrous citrate, 24g of corn starch and 1g of magnesium stearate with 100 g of the dried yoghurt powder, using a tableting machine.

[0028]

[Detail 4] The yoghurt prepared in Detail 1 was processed into dried powder by freeze-drying. A 100 capsules were prepared by filling 15 g of evenly mixed ferrous sulfate, 30 g of lactose, 70 g of microcrystalline cellulose and 100 g of the dried yoghurt powder into No.3 gelatine capsules.

[0029]

[Effect of the invention] The compound for the treatment of iron-deficiency anemia constituting this invention contains fermented milk and iron salts as its active ingredients, with the fermented milk being produced with the lactic acid bacterium Lactobacillus acidophilus. This compound has excellent

effects in improving the usability of iron and in reducing the side-effects caused by iron. The alimentation and the regulating effects on intestinal function which is basic to fermented milk can be expected, and other minerals than iron, as well as vitamins can also be supplied, making this fermented milk product highly effective against iron-deficiency anemia. That effect is especially remarkable in comparison with dried skimmed milk containing high amounts of casein, which also claims to be effective in increasing iron absorption.